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Interdisciplinary Perspectives on Sun Safety and Skin Cancer Risk: achieving consensus

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Abstract:

Importance: Overexposure to the sun is associated with increased risk of melanoma, the most commonly fatal form of skin cancer, and with non-melanoma skin cancer (NMSC), the most commonly occurring cancer in the United States. However, there are only small indications of behavioral improvements in sun protection.

Observations: Earlier attempts to identify emerging themes in skin cancer control had largely been driven by single groups of experts such as dermatologists or behavioral scientists. In contrast, 19 experts from many disciplines including dermatology, behavioral medicine, public health, anthropology, and kinesiology, along with National Cancer Institute scientific staff, possessing a wide range of expertise in other cancers, discussed knowledge gaps, interdisciplinary perspectives on sun exposure, implications for skin cancer risk and other health outcomes, and new directions. Five themes emerged: (a) Expanding the definition of risk with a need for refined categories for skin physiology and population pluralities; b) Study of co-occurrence of risky sun exposure and other health-related behaviors; c) The need for nuanced messages for at-risk populations; d) Recognition and treatment of those at risk for excessive tanning disorder; and (e) Creating scalability for sun safety interventions. Interwoven within these concepts was the compelling question of how to maximize modern technology in the community and clinical setting.

Conclusions and Relevance: It was evident that integration of technologies will be required to sharpen messages to specific populations and to integrate them within multi-level interventions. Further inter-disciplinary research should address the themes discussed with the goal of building effective and sustainable approaches. Clinicians and public health experts need greater guidance on identifying higher-risk patients within a changing environment, communicating more refined messages to encourage and motivate behavioral change, and supporting efforts in

the community and policy arenas that can coalesce to reduce the burden of skin cancer in the US and elsewhere.

Overexposure to sunlight is associated with increased risk of melanoma, the most commonly fatal form of skin cancer, and with non-melanoma skin cancer (NMSC), the most commonly occurring cancer in the United States.^{1,2} The incidence of melanoma has risen dramatically since first recorded in 1935 as has the average cost of treatment, with 5 million adults diagnosed with skin cancer estimated at an annual cost of over \$8 billion.² Recent research in genetics, anthropology and medicine indicate vulnerability to skin cancer can exist in individuals with moderately pigmented skin who consider themselves at low or no risk for skin cancer. Furthermore, evidence suggests that sun exposure has some unrecognized positive health outcomes such as benefits of vitamin D and disease risks potentiated by vitamin D deficiency involving the skeletal, nervous, cardiovascular, and immune systems.. In view of the emerging science, the 2014 Surgeon General's Call to Action to Prevent Skin Cancer ² and the National Cancer Institute's (NCI) continuing mission to make ultraviolet (UVR) protection an important priority in cancer control,³ the Board on Behavioral, Cognitive and Sensory Sciences of the National Academy of Science hosted a meeting on December 16 and 17, 2016, supported by the NCI. Experts from dermatology, behavioral medicine, public health, clinical health psychology, anthropology and kinesiology, along with NCI scientific staff, discussed knowledge gaps, interdisciplinary perspectives on sun exposure, implications for skin cancer risk and other health outcomes, and new directions.

Five themes emerged: (a) Expanding the definition of risk with a need for refined categories for skin physiology and population diversity; b) Study of co-occurrence of sun exposure and other health-related behaviors; c) The need for nuanced messages for at-risk populations; d) Recognition and treatment of those at risk for excessive tanning disorder; and (e) Creating scalability for sun safety interventions. (See Figure 1.)

Expanding the Definition of Risk: Need for Refined Categories for Skin Physiology and Population Diversity

Recognition of the carcinogenic potential of ultraviolet radiation (UVR) has led to the development of diverse strategies for reducing the risk of skin cancer ⁴, especially for individuals with lightly pigmented skin (Fitzpatrick Types I and II). Routinely practiced sun safety behavior, however, was emphasized for all people because the DNA in human skin is vulnerable to mutagenic damage potentially leading to skin cancer, regardless of constitutive pigmentation.⁵ New data from skin biology, cancer epidemiology, physiology, and skin pigmentation genetics are leading to more nuanced understanding of the reactions of human skin to UVR. This information is making possible the development of sun safety programs that emphasize assessment of individual risk based on ancestry, age, location, and lifestyle.

Despite gaps in knowledge about the biological and health consequences of UVR exposure, our current understanding of human physiology, skin reactions to UVR, and the risks of skin cancer and other diseases suggests while the harms associated with the overexposure to UVR outweigh the benefits, the positive effects of UVR exposure should not be ignored in the development of new sun safety guidelines. Recent evidence also confirms the beneficial effects of UVR, primarily in connection with cutaneous biosynthesis of vitamin D by UVRB (290-320 nm) and, secondarily, in relation to the release of vasoactive nitric oxide (NO) in the skin following exposure to UVA (320-410 nm). ^{6,7} The benefits of vitamin D and disease risks potentiated by vitamin D deficiency involving the skeletal, nervous, cardiovascular, and immune systems, and those conferred by UVA-induced NO release on the cardiovascular system (and deprivation of this effect) are imperfectly understood. ⁸ UVRUVRUVRUVR

Sun protection strategies must reflect the understanding that human skin pigmentation evolved to achieve a balance of the negative and positive effects of sun exposure, with darker skin conferring more protection against high UVA and UVRB levels near the equator and

lighter (less pigmented) skin adapted to generally lower and more seasonal levels of UVR (especially of UVRB) outside of the tropics.⁹ Skin with more eumelanin (Fitzpatrick Types V and VI) experiences less carcinogenic DNA damage from UVR exposure but also must be exposed for longer periods of time to maximize vitamin D production.⁹ Long-distance migrations, urbanization, and major changes in lifestyle, especially in the last 500 years, have affected patterns of human behavior in relation to the sun as well as the real and perceived risks of exposure. Average human lifespans also are longer now than they were centuries or millennia ago, with the effect that the potential for mutagenic DNA damage leading to skin cancer has been increased. Special attention needs to be paid to those with lighter (Fitzpatrick Type I or II) skin – who engage in incautious, episodic exposure to intense sunlight, to people – generally those with darker skin (Fitzpatrick Type V or VI) – who do not consider themselves at risk for sun-induced damage or skin cancer, and to those of lower socioeconomic groups regardless of skin color who often have lower education, cancer/skin cancer awareness, and health care access. Future precision approaches centering on the above factors and on rare (*CDKN2A/p16*) and common (*MC1R*) genes are likely to identify those at highest risk.

Study of Co-Occurrence of Sun Over-Exposure and Other Health-Related Behaviors

Behaviors that occur when people are outdoors in the sun have been largely studied in isolation from other health behaviors. For example, melanoma incidence has been associated with physical activity (ostensibly via increased risk of sunburn) but physical activity is associated with *reduced* risk for many other forms of cancer.¹⁰ Reducing risk for one disease should not come at the cost of increasing risk for another. Some health behaviors co-occur (e.g., wearing sunscreen and sunglasses), as do some unhealthy behaviors (e.g., unprotected sun exposure and alcohol intake). Particular health behaviors also can reduce the reinforcing value of other behaviors (e.g., protective clothing becomes aversive while running outside) or increase the

reinforcing value of an unhealthy behavior (e.g., use of exercise and tanning to improve body image).

Measuring the patterns and the contexts of co-occurring healthy and unhealthy behaviors can inform and increase the impact of sun safety efforts. For example, co-occurring unhealthy behaviors tend to share contexts, such as elevated alcohol consumption while vacationing,¹¹ when people may be at high risk for sunburns and unprotected sun exposure. Alternatively, people may pair healthy and unhealthy behavior because they adopt a compensatory approach (e.g., “sun exposure/tanning while exercising is ok”); or suspend their usual sun-protection behavior on “special occasions” (e.g., vacations, indoor tanning before a prom or wedding).¹² Research concerning changes in built environments and policy (e.g., creation of shade, placement of signage, and sunscreen dispensers, etc.) and their effects on sun-safety should be studied.² These examples represent new directions to increase understanding sun protection by studying physical environments, multiple health behaviors, and multiple underlying social, affective, and cognitive processes, assessing sun protection motivation and employing “bundled messaging” approaches targeting multiple health behaviors, while recognizing the specific context where they co-occur.

Physical activity is one such health-enhancing behavior deserving attention in sun safety research for it is associated with sunburn, which is reported by over 40% of adults and two thirds of teens annually.¹³ Sunburn is the best proximal biomarker of melanoma with hazard ratios rivaling that of tanning bed exposure. Athletes report that forgetting to apply and not liking how sunscreen feels during physical activity are barriers;¹⁴ protective clothing may also be perceived to reduce physical activity performance or enjoyment. Individuals may believe that an active lifestyle reduces cancer risk, negating the need for other remediation approaches. Of course, placing a high value on physical appearance may be drivers for both tanning and exercise, as may be stress reduction, another pathway by which these behaviors co-occur.

Recognition that sun protection may pose unique challenges to active individuals who vary by exercise type (e.g., competitive sports, recreational activity), skin type and age reinforces the need to study the nuanced associations among exercise, sunburn, unprotected sun exposure, and reasons for inadequate sun protection. New technologies, such as smart phones, remote sensors, electronic diaries, etc., can also improve understanding of activity. Sun safety and co-occurring behaviors can be linked together in real-time, in known physical contexts, and in social contexts.³ Further, these same devices can deliver messages that are targeted to individual locations or activities.

Finally, at the macro-level, little is known about how individual level approaches fit into the backdrop of current public health messages, which strongly encourage exercise for health promotion and disease prevention.

The Need for Nuanced Messages for At-Risk Populations

In the United States, sun safety messaging has mostly involved a “one size fits all” approach in which everyone is encouraged to restrict time spent in the sun during peak UVRR hours and to routinely wear sunscreen and protective clothing despite the heterogeneity of the population, but current messaging is mostly agnostic as to which protection strategy is best for whom and in what circumstances.¹⁵ Nuanced messaging may be more successful where population segments with specific risk profiles are targeted with tailored messages delivered in specific environments. Environmental (e.g., geographical, seasonal) and lifestyle risk factors (e.g., outdoor worker, exerciser) also have implications for sun safety messaging. Contending with varying motivations for UVR exposure including perceptions that a tan improves appearance, assists with stress relief, or provides health benefits is challenging. Messaging designed for teenage girls and young women, who are at risk for unsafe UVR exposures because of the influence of peers and celebrity examples, will be of particular importance.

A shift toward nuanced messaging, or “precision targeting,” has considerable potential. First, various risk factors can facilitate or undermine receptivity to specific protection recommendations and messaging may fail to address environments, motivations and behaviors that confer the greatest risk for any given individual. For example, reminding an office worker to wear sunscreen daily may not decrease her high-risk sunbathing during vacations. Second, decades of research in tobacco control, cancer screening, and physical activity show that people are more persuaded when messages are tailored to personal values, motivations, or other individual characteristics and risk factors.¹⁶ Sun safety messages for vacationers may need to stress simplicity to fit their desire to escape normal daily responsibilities. Finally, nuanced messages can allow individuals choice in how they protect themselves, which is critical for behavior change.¹⁷ An example of nuanced messaging is found in Australia, where solar UVR alerts are based on environmental factors such as geographic location and daily UVR Index.¹⁸

Developing nuanced health messages that are clear and not susceptible to misinterpretation among people at all levels of health literacy are challenges that require research about how and when people make sun protection decisions in real time, and how beliefs about sun exposure (e.g., sunbathing is part of relaxing vacations) influence receptivity to different messages at different times. For example, nuanced messages about using sun exposure to increase vitamin D could be perceived as encouragement to sunbathe.

Technology may facilitate delivery of nuanced messages and help personalize content based on individual risk factors, values, and motivations at the precise time an individual makes a decision relevant to sun safety in high-risk contexts. For example, wearable dosimeters can track UVR exposure and provide feedback similar to wearable devices that track physical activity. Social media platforms such as Facebook or Twitter may deliver and disseminate nuanced messages to specific population segments that could help counteract pro-tanning messaging from tanning salons and fashion magazines and improve audience reach.¹⁹ Mobile

applications could deliver “just in time” nuanced messages²⁰ based on UVR exposure and use of sun protection, shade, sunscreen, and location and time outdoors. Research exploring technology to reduce skin cancer risk is nascent, but much may be learned from more common technological applications for diet and exercise.

Recognition and Treatment of Those At-Risk of Excessive Tanning Disorder

A small proportion of the population is prone to excessive tanning behavior,²¹ making these individuals highly vulnerable to skin cancers. Persons engaging in very frequent, chronic excessive tanning share parallel behaviors and features exhibited in gambling, internet addiction, and compulsive buying.²² These include similar biological reward pathways and genetic correlates, lack of behavioral control, tolerance, continued engagement despite negative consequences, and common comorbidities.²³ Implicating biological rewards, experiments document that UVR light has reinforcing properties,²⁴ UVR exposure leads to the release of endogenous opioids,²² and tanning sessions increase blood flow to brain areas associated with the drug-induced reward system.²¹ In preclinical studies, UVR-exposed mice exhibit classic symptoms of opioid withdrawal after administration of naloxone and provide evidence for tolerance as well.²⁵ Furthermore, both tanning of the skin and up-regulation of beta-endorphin, the so-called “feel good” peptide, are most stimulated by the most carcinogenic part of the UVR spectrum.

Not surprisingly, nearly 1/3rd of tanners surveyed report difficulty quitting tanning.²³ Persons with these symptoms, which is termed “tanning disorder,” consistent with other addictions, also tend to have the *ANKK1* gene, which is associated with substance and alcohol dependence.²⁶

Recognizing that tanning disorder may be an addiction for certain persons suggests there may be potential benefits of testing pharmacological treatments that have demonstrated

efficacy for these other conditions. Typically, these medications remedy dysfunctions of the reward system mediated by the mesolimbic dopaminergic pathway, serotonergic dysfunctions, and mechanisms underlying compulsive disorders. For example, opioid antagonists (e.g., naloxone) have had efficacy in treating behavioral addictions, such as gambling disorder.²³ SSRI and SSNRI antidepressants decrease compulsive repetition and depression, a common comorbid symptom of behavioral addictions, through serotonergic regulation.²³ Mood stabilizers, such as carbamazepine, also may offer some potential.²³ Glutamatergic modulators (e.g., N-acetylcysteine, NAC) affect reward pathways and have been used successfully in treating substance addictions and have shown some efficacy with behavioral addictions, such as gambling disorder.²³ Given the consistent evidence for the efficacy of opioid antagonists and glutamatergic modulators, these agents should be considered for testing in persons who tan excessively.

Creating Scalability for Sun Safety Interventions

To achieve population-level skin cancer prevention, evidence-based interventions will need scaling-up to benefit more people on a lasting basis,²⁷ which is a Department of Health and Human Services' Strategic Plan goal.²⁸ Although several frameworks have guided intervention scale-up, the RE-AIM framework (Reach, Effectiveness, Adoption, Implementation, and Maintenance) is an illustrative framework for program dissemination that can inform the translation and public health impact of scale-up, including at organizational and individual levels.²⁹

Most interventions have focused on sun protection in community-based settings such as individual or small groups of schools, workplaces, outdoor recreation areas, and clinics.³ Unless interventions that are effective in these controlled studies are disseminated and implemented widely, we will not likely achieve sustained changes as the at-risk population ages and the costs

of skin cancer treatment rise. This will require more than replication in large populations; scaled-up interventions must lower cost and increase reach to provide greater access to benefits. To build capacity and influence the decision-makers who determine whether evidence-based interventions are adopted and implemented,²⁷ research on intervention scalability needs to examine reach, retained effectiveness, and costs.²⁹

Existing knowledge regarding skin cancer interventions at scale is limited primarily to multicomponent programs comprised of individual, policy, environment and mass media elements and through television advertising.⁴ We lack data about the potential impact of the ubiquitous digital communication technologies, such as the Internet, smartphones, and social media. Digital communication technologies can achieve large reach beyond individual settings with standardized, engaging content, and increased portability at potentially affordable costs.³⁰

Policies also can help: (a) achieve reach and scalability of skin cancer prevention interventions; (b) clarify personal/organizational responsibilities (e.g., who provides sunscreen and protective clothing) and formally direct individuals to take precautions and prompt organizations to devote resources to skin cancer prevention; (c) can overcome low perceived risk, personal preferences (e.g., tanning), and other barriers, as well as equalize gender and age differences in health practices and place skin cancer prevention on the agenda of decision makers.

Population-wide skin cancer prevention interventions, such as the SunSmart campaign in Australia or the national campaign in Denmark, provide insights into scalability that may have relevance to the United States.¹⁸ Scalability also can be studied with prospective trials; however, unlike effectiveness research that focuses mainly on changing behavior, metrics for effective scale-up should include the combination of how effective an intervention is at changing individuals' behavior when disseminated and the costs of scale-up (which are usually considerable). Scale-up methods, however, sometimes risk sacrificing intervention effectiveness to save costs. Thus, improving cost-effectiveness in terms of reach, implementation, and

behavior change should be the focus of research into scalability of skin cancer prevention interventions.

Conclusion

Common themes from the Sun Safety: Interdisciplinary Perspectives' expert meeting centered on the definition of appropriate risk groups for interventions, the co-occurrence of risky sun exposure and other health-related behaviors, the nuancing of messages for specific at-risk populations, an added emphasis on highest-risk populations such as addicted tanners, and a broader dissemination plan. It is also evident that integration of technologies will be required to sharpen and disseminate messages to specific populations and to integrate them within multi-level interventions. Further inter-disciplinary research should be conducted to address the themes discussed with the goal of building engaging, effective, and sustainable approaches to decrease the burden of skin cancer.

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Figure 1-Research Themes in Behavioral Skin Cancer Research: Understanding Risk and Developing Interventions

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